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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,509	10/18/2005	Mitsuharu Hirai	TOYA 114.010APC	4683

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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
WILDER, CYNTHIA B	
ART UNIT	**PAPER NUMBER**
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	12/28/2006	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 12/28/2006.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com
eOAPilot@kmob.com

Office Action Summary	Application No.	Applicant(s)	
	10/553,509	HIRAI, MITSUHARU	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/05 and 7/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's preliminary amendment filed on 10/18/2005 is acknowledged.

Priority

2. Acknowledgement is made of Applicant's claim for foreign priority for application 2003-114381 filed in Japan on 04/18/2003.. However, Applicant's claim of benefit is improper because Applicant did not provide a translation of the non-English priority document and statement that the English translation is accurate. MPEP 1.78, section (a)(2) requires that "If the application claims the benefit of an international application, the first sentence of the specification must include an indication of whether the international application was published under PCT Article in English (regardless of whether benefit for such application is claimed in the application data sheet)." MPEP 1.78, section (a)(5) states that "Any nonprovisional application claiming the benefit of one or more prior filed copending provisional applications must contain a reference to each such prior provisional application, identifying it as a provisional application, and including the provisional application number and if the provisional application is filed in a language other than English, *an English language translation of the non-English language provisional application and a statement that the translation is accurate*". MPEP 1.78, section (a)(5) further states that the reference and English translation of a non-English language provisional application must be submitted during the pendency of the nonprovisional application, and within the later of four months from the actual filing date of the nonprovisional application or sixteen months from the filing date of the prior provisional application." MPEP 1.78, section (a)(5) states that "except as provided in paragraph (a)(6) of this section, the failure to timely submit the reference and English language translation of a non-English language provisional

application required by 35 U.S.C. 119(e) and this paragraph is considered a waiver of any benefit under 35 U.S.C. 119(3) to such prior provisional application".

Since no translation of the priority document has been provided, Applicant has not met the requirement for benefit under 35 USC 119(e), the instant invention is afforded the instant filing date October 18, 2005.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-2 and 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shuldiner et al (5,766,851, June 16, 1998) in view of Hiratsuka et al (cited on IDS filed 7/2006). Regarding claims 1-2 and 7-8 Shuldiner et al teach a nucleic acid probe and kit (see col. 15, lines 25-31 in reference to a kit), wherein the probe has nucleotide sequence starting from the nucleotide number 183 in the nucleotide sequence of SEQ ID NO: 1 and having a length of about 16

nucleotides and wherein the probe has the nucleotide sequence of SEQ ID NOS 11 and 12 (see SEQ ID NO: 7). Shuldiner et al teach wherein the probe can be labeled with a fluorescent compound (col. 6, lines 44-49). Shuldiner et al further teaches wherein the probe may be used in hybridization assay (col. 9, lines 3-27).

Shuldiner et al differs from the instant invention in that the reference does not teach wherein the one of the ends of the nucleic acid is labeled with a fluorescent dye in which the fluorescence of the fluorescent dye decreases upon hybridization.

Hiratsuka et al provides a general teaching of labeling nucleic acid probes at one end with a fluorescence dye, wherein said dye decreases upon hybridization (Table 1). Hiratsuka teaches that theses probes are useful for detecting single nucleotide polymorphism (col. 1, third paragraph of col. 1). Hiratsuka et al teach that a probe labeled with a fluorescent dye that decreases during hybridization allows one to analyze single-base mutations based on its characteristic Tm during melting curve analysis (page 39, col. 1, last paragraph and page 37, col. 2, last paragraph). Additionally, Hiratsuka et al teach that such nucleic acid probes can be used in methods that allow rapid, highly sensitive and high-throughput analysis of single nucleotide polymorphisms (page 39, last paragraph of col. 2 and abstract).

Therefore, one of ordinary skill in the art at the time of the claimed invention would have been motivated to have modified the nucleic acid probe of Shuldiner et al to encompass a fluorescent compound, such as a fluorescent dye which decreases during hybridization for the benefit of analyzing single base mutations in a rapid, highly sensitive and high-throughput manner as taught by Hiratsuka

Regarding claim 9, Shuldiner et al teach wherein a region containing the single nucleotide polymorphism site in a nucleic acid contained in a sample is amplified to obtain the nucleic acid showing the single nucleotide polymorphism by a method using a DNA polymerase (col. 4, line 3 to col. 5, line 16).

5. Claims 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hiratsuka et al in view of Shuldiner et al as previously applied above. Regarding claim 3, Hiratsuka et al teach a method of detecting a mutation comprising performing a melting curve analysis for a nucleic acid having a single nucleotide polymorphism site by using a nucleic acid probe labeled with a fluorescent dye, and detecting the mutation on the basis of the result of the melting curve analysis, wherein the single nucleotide polymorphism is a mutation in a nucleotide sequence in a nucleic acid encoding a beta2-adrenergic receptor (abstract, page 36, third paragraph of col. 1; page 37, section 2.4, 3.1; see also "Discussion").

Hiratsuka et al do not teach wherein the single nucleotide polymorphism is a mutation in a nucleotide sequence in a nucleic acid encoding a β3-adrenergic receptor, resulting in a mutation replacing tryptophan at position 64 in an amino acid sequence of the β3-adrenergic receptor with arginine, and the nucleic acid probe is the nucleic acid probe as defined in claim 1 or 2.

Shuldiner et al teach a method for detecting a single nucleotide polymorphism, wherein the polymorphism is a mutation in a nucleotide sequence in a nucleic acid encoding a β3-adrenegic receptor, resulting a mutation replacing tryptophan at position 64 in an amino acid sequence of the β3-adrenergic receptor with arginine (abstract and col. 2, lines 51-61).

Shuldiner et al further teach wherein a nucleic acid probe comprising the sequence as depicted in SEQ ID NOS: 11 and 12 (see SEQ ID NO: 7) is utilized to analyze the mutation (col. 12, lines 6-16). Shuldiner et al teach that analysis of this mutation is important for the diagnosis of a subject having or at risk of having type II diabetes and or obesity. Shuldiner et al teach that analysis of this mutation allow more accurate diagnostic, prognostic, preventive and therapeutic regimes (col. 2, lines 51-67 and col. 3, lines 1-5).

Therefore, in view of the foregoing one of ordinary skill in the art would have been motivated to have modified the method of Hiratsuka et al to encompass detecting other mutation of the beta-adrenergic receptor, such as the beta3-adrenergic receptor, for the advantage of providing preventative and therapeutic regimes for individuals having or at a risk of having type II diabetes and/or obesity as suggested by Shuldiner et al and for the benefit of analyzing drug toxicity in patients being treated for type II diabetes and/or obesity as suggested by Hiratsuka et al.

Regarding claims 4 and 5, Shuldiner et al teach wherein a region containing the single nucleotide polymorphism site in a nucleic acid contained in a sample is amplified to obtain the nucleic acid showing the single nucleotide polymorphism by a method using a DNA polymerase (col. 4, line 3 to col. 5, line 16).

Regarding claim 6, Hiratsuka et al teach wherein a real-time PCR reaction is performed wherein the amplification is performed in the presence of a nucleic acid probe to analyze the single nucleotide polymorphism (page 37, section 2.4).

Prior art

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Ranade et al (Genome Research, vol. 11, pages 1262-1268, 2001) teach a method of analyzing the single nucleotide polymorphism resulting in a mutation replacing tryptophan at position 64 in an amino acid sequence of the Beta3-adrenergic receptor with arginine using the high-throughput TaqMan assay that utilizes nucleic acid probes comprising fluorescent dyes.

Conclusion

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Cynthia B. Wilder, Ph.D.
Patent Examiner
Art Unit 1637

12/21/2006